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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/682,496	10/09/2003	Xiao-Yi Xiao	SYR-HDAC-5003-U	8276
32793	7590	09/13/2006		
TAKEDA SAN DIEGO, INC. 10410 SCIENCE CENTER DRIVE SAN DIEGO, CA 92121				
			EXAMINER FREISTEIN, ANDREW B	
			ART UNIT 1626	PAPER NUMBER

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/682,496

Applicant(s)

XIAO, XIAO-YI

Examiner

Andrew B. Freistein

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 10,16-36,38-50 and 54-67 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 10,16-36,38-50 and 54-67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 8/25/06.

- 4) ☒ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. 20060907.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This communication is in response to the Request for Continued Examination (RCE) filed on 08/25/2006.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under Ex Parte Quayle, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114.

Applicant's submission has been considered and has been entered. Claims 10, 16-36, 38-50 and 54-67 are pending. Claims 1-9, 11-15, 37 and 51-53 were cancelled.

#### ***Information Disclosure Statement***

Applicant's information disclosure statement (IDS), filed on 08/25/2006, has been considered. Please refer to Applicant's copies of the 1449 submitted herewith.

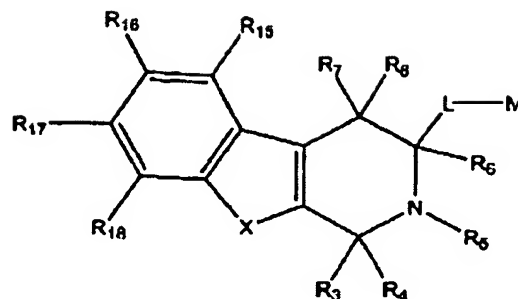
#### ***Restriction Requirement***

The claim amendments filed 8/25/2006 fail to limit the scope of the elected invention according to the Office Action mailed 09/30/2005. Examiner has further broadened the scope of the search. The section is reiterated below:

#### **Elected and Examined Subject Matter**

The scope of the invention of the elected and the examined subject matter is as follows:

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Compounds of the Formula of Claim 10,

wherein according to the claims:

**R<sub>3</sub> and R<sub>4</sub>** are each independently H, alkyl, aminoalkyl, oxaalkyl, aromatic ring, cyano, a carbonyl group, and a thiocarbonyl group;

**R<sub>5</sub> and R<sub>6</sub>** are each independently H, alkyl, aminoalkyl, oxaalkyl, aromatic ring, cyano, carbonyl group, thiocarbonyl, or sulfonyl group;

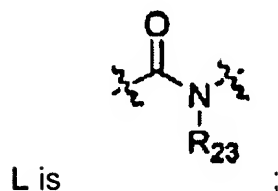
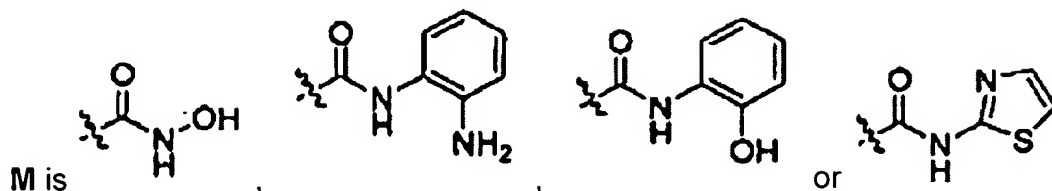
**R<sub>7</sub> and R<sub>8</sub>** are each independently H, alkyl, aminoalkyl, oxaalkyl, aromatic ring, alkoxy, aryloxy, alkylamino, arylamino, alkylthio, arylthio, acylamino, sulfonylamino, nitro, cyano, halogen, hydroxyl, thiol, amino, carbonyl group, or thiocarbonyl group;

**R<sub>15</sub>, R<sub>16</sub>, R<sub>17</sub> and R<sub>18</sub>** are each independently H, alkyl, aminoalkyl, oxaalkyl, aromatic ring, alkoxy, aryloxy, alkylamino, arylamino, alkylthio, arylthio, acylamino, sulfonylamino, nitro, cyano, halogen, hydroxyl, thiol, amino, a carbonyl group, and a thiocarbonyl group;

**X** is NR<sub>14</sub>;

**R<sub>14</sub>** is H, hydroxyl, alkyl, aromatic ring, alkoxy, aryloxy, a carbonyl group, a thiocarbonyl group, or a sulfonyl group;

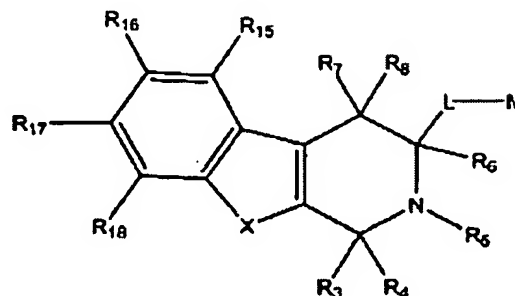
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$R_{23}$  is  $C_{1-10}$ alkyl; and

### Non-Elected and Non-Examined Subject Matter

The scope of the invention of the non-elected and non-examined subject matter is as follows:



Compounds of the Formula of Claim 10,

wherein according to the claims:

$R_3$  and  $R_4$  are taken together to form a ring, which is optionally substituted;

$R_5$  and  $R_6$  are taken together to form a 3, 4, 5, 6, 7 or 8 membered ring, which is optionally substituted;

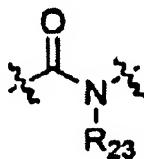
$R_7$  and  $R_8$  are taken together to form a carbonyl group, thiocarbonyl, imine, alkene, and ring;

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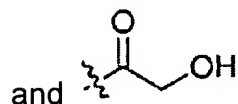
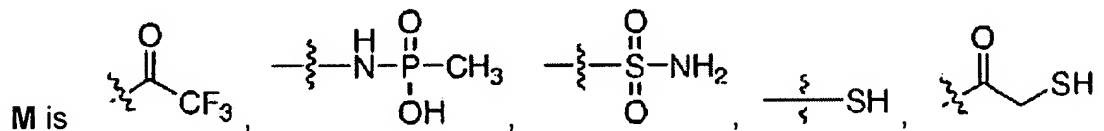
**R<sub>6</sub> and R<sub>7</sub>** are taken together to form a 3, 4, 5, 6, 7 or 8 membered ring, which is optionally substituted;

**R<sub>15</sub> and R<sub>16</sub>; R<sub>16</sub> and R<sub>17</sub>; and/or R<sub>17</sub> and R<sub>18</sub>** are each taken together to form a 3, 4, 5, 6, 7 or 8 membered ring, which is optionally substituted;

**X** is O, or S;



**L** is a group other than ;



As a result of the election and the corresponding scope of the invention, identified supra, the remaining subject matter of Claims 10, 16-36, 38-50 and 54-67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups such as furan, thiofuran, pyrrole, isoimidazole, pyrazine, benofuran, isoquinoline, cinnoline, etc. which are chemically recognized to differ in structure, function, and reactivity.

Therefore, the subject matter which was withdrawn from consideration as being non-elected subject matter materially differs in structure and composition from the

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examined subject matter so that a reference which anticipates the examined subject matter would not render obvious the non-elected subject matter.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**(Pending Rejections)** Claims 10, 16-38 and 49-65 were rejected under 35

U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is withdrawn with respect to variable "L."

**(New Rejection)** Claims 10, 16-36, 38-50 and 54-67 are rejected under 35

U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In Claim 10, 26, 33-35, in the definitions of R3, R4, R5, R6, R7, R8 R15, R16, R17, R18 and X, the variables are "unsubstituted or further substituted through available valencies." However, there is no indication what these substitutions are. Further, the specification does not provide a definition of the possible substituents.

Claims 16, 17, 20-25, 27-32, 61-63 and 66 are drawn to a "substituted or unsubstituted" ring. The specific substituents are not identified in the claims and the specification does not provide a definition of what the substituents are.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**(Pending Rejection)** Claims 10 and 16-65 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is maintained and newly added claims 66-67 are also rejected.

Applicant traverses the rejection of the variable "L" asserting that one of ordinary skill in the art would fully appreciate that the backbone atoms of L are the atoms that form the most direct chain of atoms and bonds (i.e. the fewest atoms and bonds) between the M substituent and the carbon ring atom alpha to L. Specifically, the backbone atoms serve to extend M "a sufficient distance away from the remainder of the inhibitor so as to allow [M] to interact with the zinc ion while the remainder of the inhibitor interacts with hydrophobic regions in the binding pocket of the histone deacetylase."



Examiner respectfully disagrees with Applicant. The definition of "L" was amended to state:

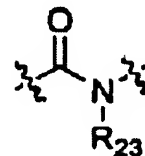
L is a leader group moiety separating the M substituent from the carbon ring atom alpha to L, wherein the number of backbone atoms of the leader group moiety separating the M substituent from the carbon ring atom alpha to L is between 3 and 12.

The claim continues to be indefinite, because it does not define the metes and bounds of the claim. Applicant asserts that the backbone atoms serve to extend M "a sufficient distance away from the remainder of the inhibitor so as to allow [M] to interact with the zinc ion while the remainder of the inhibitor interacts with hydrophobic regions in the binding pocket of the histone deacetylase." The function of the atoms does not define the atoms. One of ordinary skill in the art can appreciate what the L substituent does, but one of ordinary skill in the art cannot appreciate what the L substituent is. The claim is drawn to "a compound." The claim is not drawn to a method of interacting with a zinc ion. What is the compound that Applicant claims is his invention?

Applicant contends that the specification teaches multiple variations of leader groups that fall within the scope of the present invention, such as the embodiments shown in Figure 2B, and Figure 2(c) (depicted in claims 38 and 54-56). Examiner appreciates these specific embodiments. At least one of these embodiments must be inserted into claim 1 in order to identify the compound that applicant claims as his invention. At present, L is defined as an ambiguous and indefinite moiety and the specification defines this moiety in terms of a function rather than a structure. In order to overcome this rejection, the claims must be amended to specifically point out and

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distinctly claim the compound that applicant regards as his invention. For example, L

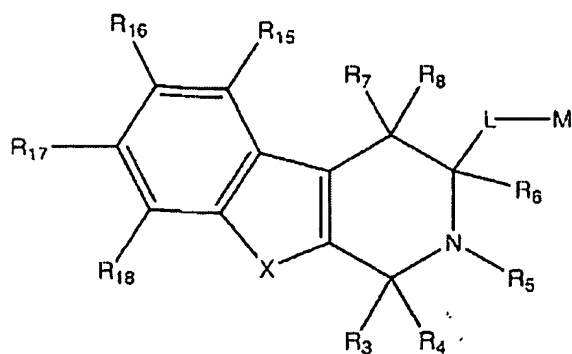


could be amended to be the first moiety depicted in claim 38,

Alternatively, L could be amended to be a moiety selected from group consisting of those depicted in claim 38. However, Applicant should note the scope of the elected and examined subject matter and the amendment is subject to further restriction (see "Elected and Examined Subject Matter" section above).

**(New Rejections)** Claims 10 and 16-36, 38-50 and 54-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(1) Claim 10 is drawn to a compound "comprising the formula



." The term "comprises" is an open-ended transition phrase and is improper for Markush-type claim language. Currently, claim 1 is drawn to a compound of the formula and anything else under the sun. The term "comprising" should be deleted and the word "of" should be inserted. MPEP 2111.03 & 2173.05(h).

(2) Claim 18 recites the limitation "further comprises a substituent selected from the group consisting of alkyl, aromatic ring, cyano group, halogen, and carbonyl group." The term "comprises" is an open-ended transition phrase and is improper for Markush-type claim language. What else does the compound comprise? The claim should be amended to state "A compound...wherein the C<sub>1</sub>-C<sub>10</sub> alkyl, amioalkyl, or oxalalkyl is substituted with a substituent selected from the group consisting of..."

(3) Claim 19 recites the limitation "further comprises a substituted or unsubstituted aromatic ring." The term "comprises" is an open-ended transition phrase and is improper for Markush-type claim language. What else does the compound comprise? The claim should be amended to state "A compound...wherein the C<sub>1</sub>-C<sub>10</sub> alkyl, amioalkyl, or oxalalkyl is substituted with a substituted or unsubstituted aromatic ring."

(4) Claims 10, 16-36, 38-50 and 54-67 each state "substituted or unsubstituted" variables. However, none of the substituents are identified and the specification does not provide what the substituents are.

(5) Claims 54-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 54-56 are drawn to a compound according to claim 10 wherein a portion of the backbone atoms of L are substituted to form a member of the group consisting of..." Previously, the groups listed in claims 54-56 were the alternatives of L. However, now the claims are drawn to the substituents of L. These optional substituents are indefinite, because it is unclear what portion of the

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backbone creates the substituent. In order to overcome this rejection, Applicant must show a chemical structure of L and then a group of the optional substituents, which identifies the location of the substitution. In the event that Applicant intended to further identify "L," then the claims should be amended to state "A compound according to claim 10, wherein L is selected from the group consisting of..."

### ***Claim Objections***

Claims 10, 16-36, 38-50 and 54-67 are objected to as containing non-elected subject matter.

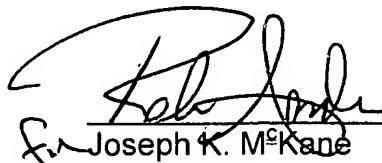
### ***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M<sup>c</sup>Kane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Andrew B. Freistein  
Patent Examiner, AU 1626



Joseph K. M<sup>c</sup>Kane  
Supervisory Patent Examiner, AU 1626  
Date: September 12, 2006